PATENT
Attorney Docket No. A-63708-5/RFT/TAL/CYO
Attorney Client Matter No. 465840-00245

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

BUELOW *et al.*

Serial No. 09/515,582

Filed: February 29, 2000

For: *METHODS FOR ENHANCING GRAFT SURVIVAL BY MODULATING HEME OXYGENASE ACTIVITY*

Examiner: Li, Q.

Art Group No. 1632

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231 on:

Date: April 3, 2003

Signature Beverly Dynes
Beverly Dynes

DECLARATION PURSUANT TO 37 C.F.R. § 1.132

Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Suhasini Iyer, Ph.D., do hereby declare as follows:

1. I am a Director of PreClinical Research and Development at Sangstat Medical Corporation, a biotechnology company located in Fremont, CA.

2. I am a co-inventor with Roland Buelow and Jacky Woo of the invention claimed in U.S. Patent application Serial No. 09/515,582 (referred to hereafter as "the application").

3. I have read and understand the Office Action in this case dated October 3, 2002. I am familiar with Examiner's position asserting nonenablement of extending graft survival by administering to a recipient following organ transplant a nucleic acid with at least about 80% nucleic acid sequence identity to human heme-oxygenase I gene.

4. The specification on page 25 (lines 1-5) discloses extension of graft survival by administration of the nucleic acid after transplantation. At the time of filing of the application, it was known that administration of cobalt protoporphyrin to a transplant recipient extends graft survival for periods similar to those observed for administration of the protoprophyrin into an organ prior to transplant. These results are described in U.S. Patent No. 5,756,492.

5. Given the disclosure in the present application showing a correlation between graft survival and induction of heme-oxygenase levels by cobalt protoporphyrin (Example 1), and clear demonstration that administering a nucleic acid having at least about 80% homology to the human heme-oxygenase I gene to directly modulate heme-oxygenase levels extends graft survival, a person knowledgeable in transplant studies would reasonably conclude that administering the nucleic acid following organ transplantation would also extend graft survival.

6. As confirmation of the descriptions in the specification, provided herein as Attachment A is the results of studies performed at Sangstat Medical Corporation (Fremont, CA) and Institut National de la Sante Et de la Recherche Medicale (Cedex, France) using a rat cardiac transplant model. Specifically, heterotropic heart grafts were performed in male Lewis 1W rats mismatched for the entire MHC region. The figure shows that administering adenoviral vector containing human heme-oxygenase I gene (Ad HO-I) to a recipient subsequent to organ transplant extends graft survival. Administration into either the transplanted heart (IG injection), the hind limb muscle (IM injection), or via intravenous route (IV injection) into the recipient prolongs organ survival as compared to untreated animals or animals treated with control vector lacking heme-oxygenase gene (Add1324). Intravenous administration of Ad HO-1 significantly prolongs organ survival. These results support descriptions set forth in the application that administration of the recited nucleic acids to a transplanted organ or a recipient subsequent to organ transplant extends graft survival.

7. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with knowledge that the making of willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States

Code and that such willful statements may jeopardize the validity of the application or any patent issuing thereon.

Date: April 3, 2003

Signed: Suhasini

Suhasini Iyer, Ph.D.
Sangstat Medical Corporation